

protocol so that the collective experience of many institutions will contribute to the further understanding and better management of such cases. Much more needs to be known if women with renal transplants are to be carefully selected to enjoy pregnancy and parenthood with maximum benefit to themselves and their offspring. We doubt, however, if a decision to undertake a transplant should ever be based on a desire for parenthood.

J M DAVISON  
T LIND

MRC Reproduction and Growth Unit,  
Princess Mary Maternity Hospital

D N S KERR

Department of Medicine,  
Royal Victoria Infirmary,  
Newcastle upon Tyne

<sup>1</sup> Davison, J M, Lind, T, and Uldall, P R, *British Journal of Obstetrics and Gynaecology*. In press.

<sup>2</sup> Merkat, J R, et al, *Journal of the American Medical Association*, 1971, **216**, 1749.

### Hypoglycaemia in children undergoing adenotonsillectomy

SIR,—Those constantly concerned with eliminating the risks associated with operations on the tonsils and adenoids will be grateful to Dr C J H Kelnar for his contribution (27 March, p 751). He states, however, "It is not unreasonable to suppose that some of the 15 to 20 children who die each year after adenotonsillectomy die from the effects of unrecognised hypoglycaemia." It may well be that some children die from this cause, but the total number of deaths per annum is very much less than quoted. In the five years 1964-8 the annual number of deaths from this operation had dropped to little less than seven and in 1970 figures from the Office of Population Censuses and Surveys showed that there was but one death and that from adenoidectomy without tonsillectomy.

In recent years improved management and a steady reduction in the number of operations have combined to reduce the mortality rate to very small proportions. Nevertheless, the utmost vigilance is still required, which should certainly take into account the important factor publicised by Dr Kelnar.

STUART MAWSON

London W1

### Thyrotoxicosis induced by iodine in food

SIR,—I enjoyed reading the authoritative paper by Drs J C Stewart and G I Vidor (14 February, p 372) in which they pointed out that increased frequency of thyrotoxicosis was observed after addition of iodine to the diet in northern Tasmania. It has been suggested<sup>1</sup> that the development of endemic goitre is related to a balance between thyroid-stimulating hormone (TSH) production and thyroid size. Iodine deficiency thus leads to decreased thyroid hormone production, which in turn causes increased TSH secretion and increased thyroid size until there is enough thyroid tissue to trap a proportion of circulating iodine large enough to maintain normal hormone levels. Any increase in iodine intake in such persons thus causes a trend towards thyrotoxicosis because the thyroid is adjusted to a higher than normal degree of iodine utilisation.

In a goitre region with iodine deficiency

any increase in iodine intake must thus lead to an initial increase in the frequency of thyrotoxicosis, as was shown by the authors. If, however, iodine intake in the area becomes permanently adequate through iodine prophylaxis the frequency of thyrotoxicosis would eventually decrease. The increased incidence of thyrotoxicosis after iodine is added to food is thus a consequence of iodine deficiency.

An accumulation of thyrotoxicosis patients in the generation in which iodine prophylaxis is begun seems to be the price to pay for normal thyroid physiology in the following generations. When basal iodine intake is sufficient to maintain normal hormonal balance occasional increases in iodine intake should not cause any increased frequency of thyrotoxicosis. In other words, bread and milk would still be preferable to cakes and ale—albeit not for the goitrous.

PETER WAHLBERG

Department of Internal Medicine,  
Aland Central Hospital,  
Mariehamn,  
Finland

<sup>1</sup> Becker, F O, in *Year Book of Endocrinology* 1974, p 198. Chicago, Year Book Medical Publishers, 1974.

### IUD and congenital malformation

SIR,—One must never dismiss reports of possible iatrogenic damage to the developing fetus. But the two cases described by Dr Herbert Barrie (28 February, p 488) provide little support for a cause-and-effect link between copper-containing intrauterine devices (IUDs) and limb-reduction defects. As suggested by Dr Robert Snowden (27 March, p 770), conception and organogenesis in the second case may have occurred after expulsion of the IUD. Moreover, the lead content (0.01-1%) of the Gräfenberg ring in the first case may have caused the malformation rather than the copper—if the association was not coincidental. The chief problem is that the relevant denominator is unknown—that is, the size of the population fitted with Gräfenberg rings and the number of in-situ pregnancies occurring. In Dr Snowden's study<sup>1</sup> these figures are available, and it is reassuring that no congenital abnormalities were reported among the 21% of 317 pregnancies reaching viability.

What about devices which contain much more (about 90 mg) of copper? The following results are by courtesy of the medical department of Searle Laboratories, High Wycombe, and relate solely to the Copper-7 device (Gravigard). In two international studies there were 20 684 insertions, and 714 pregnancies with Copper-7 devices in situ at conception have been reported. Of these, 167 reached viability, 8% were lost to follow-up, and the remainder were ectopic or ended in spontaneous or induced abortion. Normal babies resulted from 159 pregnancies. No details were given about three infants and the remaining five had the following malformations: (1) permanent bald spot; (2) bilateral congenital eyelid ptosis; (3) fatty tumour on the back; (4) congenital dislocation of hip (breech delivery); (5) lumbosacral meningocele and bilateral talipes—neonatal death at seven days. If the three doubtful cases are included the incidence of congenital defects was eight out of 167 or 4.8% (very close to the figure quoted by Dr Barrie as the expected rate).

Note that no limb-reduction defects were reported. However, in addition to the above cases from a defined population there have

been 23 pregnancies reaching viability and reported spontaneously by doctors to Searle's—all from the United Kingdom. Nineteen normal infants were reported and of the four cases of congenital abnormality one was that described by Miss P C Leighton and her colleagues (24 April, p 949) with multiple limb-reduction deformities. This is the only such case reported in Britain since the Gravigard was first marketed in September 1972. The size of the population at risk from which the case comes is unknown. (A very approximate indication may be obtained, based on the fact that about 376 000 of these devices have been sold within the British Isles.)

In conclusion, I would agree with the last paragraph of Dr Barrie's article. The likelihood of spontaneous abortion, which may be septic,<sup>2</sup> and of other dangerous complications of pregnancy and delivery<sup>3,4</sup> is such that most authorities would agree that "serious consideration should be given to terminating pregnancies with a retained intrauterine device" on maternal grounds. But on the figures given here the teratogenic risk to the fetus if a Copper-7 device was in use would not be added grounds for legal abortion.

JOHN GUILLEBAUD

Nuffield Department of Obstetrics  
and Gynaecology,  
John Radcliffe Hospital,  
Oxford

<sup>1</sup> Snowden, R, *FPA Medical Newsletter*, No 59, 1976, p 1.

<sup>2</sup> Eisinger, S H, *American Journal of Obstetrics and Gynecology*, 1976, **124**, 393.

<sup>3</sup> Vessey, M P, et al, *Lancet*, 1974, **1**, 495.

<sup>4</sup> Steven, J D, and Fraser, I S, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1974, **81**, 282.

### Control of menstrual bleeding during haemodialysis

SIR,—Over the past two years a new intra-uterine device (IUD) releasing progesterone (Progestasert) has been used for contraception.<sup>1-3</sup> During these studies it was observed that total menstrual blood loss decreased and removals of the device for bleeding were reduced.

Patients with renal disease awaiting transplantation and undergoing haemodialysis often experience heavy and troublesome menstrual periods. Control of these periods with continuous hormone therapy (usually a combined oestrogen and progestogen pill) often gives rise to side effects. In an attempt to reduce these side effects we have used the progesterone IUD for menstrual cycle control in four patients awaiting renal transplantation. All four had chronic glomerulonephritis with varying periods of amenorrhoea during the progression of their kidney disease. With dialysis all developed heavy periods requiring treatment. Norethisterone 30 mg/day controlled two patients' bleeding but gave other unpleasant side effects, such as a bloated feeling and water retention. On reduction of the dose to 10 mg/day both experienced troublesome breakthrough bleeding. Of the other two patients, one had heavy periods with norethisterone and the other severe breakthrough bleeding. All four patients experienced troublesome menstrual side effects when combined oral contraceptive preparations were used.

The progesterone IUD was easily inserted in all four patients. Following insertion all four had regular menstrual cycles with accept-

able amounts of blood loss. The total length of menstrual bleeding and the amount (number of tampons used) was reduced in all cases. One patient noted some intermenstrual spotting, but this was acceptable.

The first two patients have been followed up for 11 and 16 months respectively and are alive and well, still with regular menstrual cycles and acceptable blood loss. The third patient was followed up for seven months and during this time had regular cycles with no side effects; four months after insertion she had a kidney transplant and three months later died from a massive gastrointestinal haemorrhage. The fourth patient was seen for nine months after IUD insertion; after five months she also had a kidney transplant and four months later died from pneumococcal pneumonia. These two deaths were not related to the IUD use.

We conclude from this small series that the progesterone IUD offers definite advantages for patients undergoing haemodialysis who have heavy periods. In contrast to the use of systemic steroids intrauterine progesterone produces regular cycles with acceptable menstrual blood loss.

J NEWTON  
S A SNOWDEN  
VICTOR PARSONS

Department of Obstetrics and  
Gynaecology,  
King's College Hospital Medical School,  
London SE5

<sup>1</sup> Pharriss, B B, *et al*, *Fertility and Sterility*, 1974, **25**, 915.

<sup>2</sup> Martinez-Manatou, J, *et al*, *Fertility and Sterility*, 1974, **25**, 922.

<sup>3</sup> Rosado, A, *et al*, *Contraception*, 1974, **9**, 39.

### Laparoscopic removal of IUDs from the abdomen

SIR,—Perforation of the uterine wall by intra-uterine contraceptive devices (IUDs) is an uncommon but not rare occurrence. With the increasing popularity of the IUD the incidence of this complication will quite possibly increase.

We have recently seen two such cases. Both presented with diffuse acute low abdominal pain which had started three or four days after insertion of an IUD (Lippes loop, size C, in one and Copper-7 (Gravigard) in the other) by an experienced general practitioner. The pain had gradually become more severe over five or six days until admission. Both patients were multiparous and apparently had normal pelvic anatomy at insertion of the IUD. On examination there was generalised lower abdominal tenderness and marked cervical excitation. The thread of the IUD could be neither seen nor felt in the cervix.

Removal was by laparoscope, using a method basically similar to that described by Steptoe,<sup>1</sup> under general anaesthesia. The thread attached to the IUD was in both cases visualised by manipulation of the uterus by means of Hulka forceps in the cervix. The thread was then grasped with Palmer forceps passed into the abdomen through a trocar inserted at the junction of the medial third and the lateral two-thirds of a line joining the umbilicus and right anterior superior iliac spine. The forceps and trocar were then withdrawn together, and the IUD, still grasped by its thread with the forceps, was manipulated through the tiny incision made by insertion of the trocar. In both cases the site on the posterior aspect of the uterus at which perforation had occurred was scarcely noticeable. The only other pathological finding in the abdomen was a pool of "old" blood, about 20-30 ml in volume, in the pouch of Douglas. In both cases the patient was able to be discharged the following day.

These cases illustrate the use of laparoscopy as a therapeutic as well as diagnostic process

and also emphasise the importance of checking the position of the IUD in patients presenting with low abdominal pain who have had one of these devices fitted.

DEREK J PEARCE

West Kent General Hospital,  
Maidstone

<sup>1</sup> Steptoe, P C, *Laparoscopy in Gynaecology*, 2nd edn. Edinburgh, Livingstone, 1975.

### IUDs and fibrinolysis

SIR,—In your leading article (7 February, p 304) you suggest that the mechanism of the tendency of intrauterine contraceptive devices (IUDs) to cause heavy periods might not be completely separable from the mechanism of the device's contraceptive action.

We examined fertilised rat ova histochemically for their fibrinolytic activity.<sup>1</sup> Activity was found during tubal passage but disappeared at implantation. Simultaneously the fibrinolytic activity of the endometrium disappeared. It is well known that inhibition of fibrinolysis in organ and cell culture on clotted substrates promotes adhesion and growth.<sup>2</sup> Absence of fibrinolytic activity might thus be a prerequisite for implantation of the zygote. In the light of these observations it is of interest to note that IUDs raise the fibrinolytic activity in the endometrium, which, in contrast to that of non-users, is localised to the superficial cell layer.<sup>3</sup>

The disappearance of endometrial fibrinolytic activity at the time of decidualisation prompted us to study the human decidua in tissue culture for inhibitors of fibrinolysis. We used a method in which tissue explants are cultured in the presence of, but not in contact with, a preformed standard plasminogen-contaminated fibrin clot. Urokinase added to the culture medium degrades the fibrin with consequent accumulation of stable fibrin degradation products (FDP) in the medium. The amount of FDP is assessed immunochemically. When inhibitors are released from the cultured explants they will inhibit the formation of FDP.<sup>4</sup> The results are given in the table.

*Inhibition of urokinase by decidua in organ culture. Mean value of two cultures. Each value denotes FDP content in µg/l of Parker medium*

	Days of culture		
	1	2	3
Urokinase 3.0 U/ml alone	153	228	448
Urokinase 3.0 U/ml + decidua	15	69	120
Urokinase 1.5 U/ml alone	27	87	195
Urokinase 1.5 U/ml + decidua	7	22	38
Urokinase 0.75 U/ml alone	1.5	15	60
Urokinase 0.75 U/ml + decidua	0	0	5
Decidua alone	0	0	1.5

We also examined decidua cultures for their influence on the fibrinolytic activity of rat ova. When rat ova were incubated on fibrin slides without culture medium or with addition of fresh medium the mean lytic area was found to be  $90 \times 10^3 \mu\text{m}^2$ . On the slides to which human or rat decidua culture medium had been added to the fibrin film the lytic area never exceeded the area of the ovum—that is,  $< 18 \times 10^3 \mu\text{m}^2$ .

IUDs medicated with inhibitors of fibrinolysis have been claimed to decrease the incidence of intermenstrual bleeding as well as heavy periods. However, the possible inter-

ference of such treatment with the contraceptive effect of the device should be borne in mind.

B ÅSTEDT  
P LIEDHOLM

Department of Obstetrics and  
Gynaecology,  
University of Lund,  
Allmänna Sjukhuset,  
Malmö, Sweden

<sup>1</sup> Liedholm, P, and Åstedt, B, *International Journal of Fertility*, 1975, **20**, 24.

<sup>2</sup> Ingemansson-Nordqvist, B, and Källén, B, *Experimental Cell Research*, 1961, **21**, 232.

<sup>3</sup> Larsson, B, Liedholm, P, and Åstedt, B, *International Journal of Fertility*, 1975, **20**, 77.

<sup>4</sup> Åstedt, B, Pandolfi, M, and Nilsson, I M, *Proceedings of the Society for Experimental Biology and Medicine*, 1972, **139**, 1421.

### Supervision of repeat prescribing

SIR,—As director of the research centre from which the paper by Mrs S M Shaw and Mr L J Opit comes I am naturally distressed at the astonishment, hilarity, and anger of the practitioners involved (20 March, p 713). The authors themselves are, of course, responsible for the views expressed in the paper and I would not wish to speak for them, but I think I must in fairness reply on behalf of a number of other loyal and hardworking collaborators and say how much I regret unwarranted public castigation of their work.

I appreciate that these comments arise from the hot sense of injustice which the partners feel, and this partly from their failure to receive their transcript of the paper. We suppose this error must have occurred in this office and must accept responsibility, although we are now unable to trace events because of a burglary with much destruction and subsequent disorganisation. Absence of acknowledgements in the paper was due to the partners' request for non-identification following their perusal and commentary upon earlier accounts of the work and not to any intended slight.

There is one other point I must put straight. It is possible to read one of the sentences in the partners' letter to imply that Mrs Shaw changed the treatment of one of the patients. This was raised in discussion between ourselves and the practice, when I was present, and it was explained that a locum doctor changed the treatment when informed of the situation. This was not doubted by the partners at the time and I hope they are not doubting it now. Perhaps I am over-sensitive in treating a bit of ambiguous English as something which could be seen as an innuendo.

E G KNOX

Health Services Research Centre,  
Department of Social Medicine,  
University of Birmingham

### Disposable bacteriological loops and vaginal discharge

SIR,—The investigation of a vaginal discharge involves sample taking from the urethra, cervix, and vagina for Gram staining, culture, and wet-film microscopy. The standard bacteriological swab has certain drawbacks. It is too big to enter the urethra without pain and may be too big to enter the cervical canal. Any Gram films made may be obscured by carbon particles if a charcoal-coated swab is used. A common alternative is the platinum